



The increase in body mass index observed after lung volume reduction may act as surrogate marker of improved health status

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KEYWORDS

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Summary Objective: To assess the effects of lung volume reduction surgery (LVRS) on body mass index (BMI).

Methods: Prospective data was collected on a series of 63 patients undergoing LVRS (bilateral in 22 patients, unilateral in 41 patients). Median age was 58 (41–70) years. The peri-operative effects of LVRS on BMI, lung function and health status (assessed by SF 36 questionnaire) were recorded at 3, 6, 12 and 24 months.

Results: We found an overall increase in BMI after LVRS, which was significant up to 2 years. These changes correlated with the changes in FEV₁ ($R = 0.3$, $P < 0.01$ 6 months after LVRS) and diffusing capacity for carbon monoxide (DLCO) ($R = 0.5$, $P < 0.01$ 6 months after LVRS). At 6 months, when the best results in health status were found, the patients were divided in a responders group (improved SF 36 score) and a non-responders group (same or worse SF 36 score) for each of the 8 domains of the SF 36. In 6 domains the non-responders showed no increase in BMI. In 6 domains the responders showed a significant increase in BMI.

Conclusion: LVRS significantly improves postoperative BMI, which correlates with improvements in DLCO and reflects changes in health status.

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Introduction

Nutritional depletion has been reported in one-third of patients with stable COPD¹ and when expressed as percentage of ideal body weight, is significantly correlated with FEV₁ and diffusing capacity for carbon monoxide (DLCO).² Underweight patients experience a higher degree of dyspnoea³ and a low body mass index (BMI) is associated with increased risk of mortality.⁴

The observed weight loss in COPD is the result of a decrease in body cell mass. Muscle mass is the largest component of body cell mass and is indirectly measured as fat-free mass. In addition emphysematous patients not only have a lower fat-free mass but also a lower fat mass compared to chronic bronchitis patients.⁵ There have been conflicting results from studies regarding the effect of nutritional supplementation in patients with COPD but a meta-analysis found that nutritional supplementation did not have any effect on pulmonary function, body weight or BMI.⁶ In contrast, several surgical series have reported an increase in weight after lung volume reduction

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surgery (LVRS).⁷⁻⁹ One study showed this to be due to an increase in fat-free mass.⁸

Lung volume reduction has also been shown to result in improvements in respiratory physiology and health status.^{10,11} We wanted to test the hypothesis that increased BMI after LVRS correlates with improved pulmonary function and more importantly with the observed improvement in health status.

Patients and methods

All patients referred for LVRS were assessed by a multi-disciplinary selection panel comprising: a respiratory physician, a physiotherapist, two radiologists and two surgeons. Patients underwent physical examination including measurements of weight and height, basic spirometry, plethysmography, arterial blood gas analysis, chest radiography, computed tomography and radionuclide ventilation/perfusion scintigraphy.

Selection criteria

Patients had to have significant symptomatic dysfunction judged by the modified MRC dyspnoea scale as grade 3–5.¹² Spirometric inclusion criteria consisted of an FEV₁ of 15–40% of predicted; residual volume (RV) in excess of 200% of predicted; total lung capacity (TLC) greater than 120% of predicted and a RV/TLC ratio over 60%. Anatomical criteria included the presence of heterogeneous emphysema with target areas of severe emphysema on CT scan. “Physiological” heterogeneity was assessed on radionuclide scintigraphy. This was quantitated by calculating the “Q score” as determined by the ratio of perfusion in the target zone to the total lung perfusion.^{13,14} Patients with target areas in either upper or lower lobes were included.

Exclusion criteria included single large bullae, hypercapnia ($p\text{CO}_2$ greater than 7 kPa), greatly reduced diffusion capacity (KCO less than 25% of predicted).

All patients underwent preoperative pulmonary rehabilitation. Patients who could not complete a distance of 150 m in a shuttle walk test did not proceed to operation. Rehabilitation was carried out as a 7-week out-patient or 2-week in-patient programme.

Before surgery but after rehabilitation, health status was assessed using the Medical Outcomes Survey Short Form 36-item questionnaire (SF 36).¹⁵ This is a generic health status questionnaire in

which 36 questions covers 8 health domains; physical functioning, social functioning, role limitations due to physical problems, role limitations due to emotional problems, mental health, energy/vitality, pain and general health status. For each domain scores are transformed to range from 0 (worst possible health status) to 100 (best possible health status).

Surgical approach

At the start of the series all operations were performed bilaterally via median sternotomy. Subsequently one of the surgeons adopted a policy of bilateral video-assisted thoracoscopic surgery (VATS) and latterly a policy of staged unilateral VATS. All operations entailed stapled resection of functionless areas of lung using bovine pericardial buttresses (Peri Strips, Bio-Vascular, MN) as described previously.¹⁰

Postoperative follow-up

Patients were reviewed as outpatient clinic at 3, 6, 12 and 24 months post-LVRS. Patients underwent detailed spirometry and plethysmography. DLCO was measured by single-breath technique (assumed normal haemoglobin). Weight (indoor clothes) and height were recorded routinely to determine the normal values of physiological measurements for each patient. All values of respiratory physiology are given as percent of predicted normal values. At each visit patients completed SF 36 questionnaires.

Statistical analysis

The relationships between preoperative and postoperative variables were assessed using paired and unpaired Student's *t*-test. Correlations were determined using Pearson correlation coefficient. A *P*-value less than 0.05 was considered to indicate a statistically significant difference.

Results

Preoperative characteristics

Prospective data was collected of 75 patients. Patients who had not yet reached 3 months post surgery (3 patients) or who had died (9 patients) before the 3 months follow-up were excluded from this series. Data was available for 63 patients at 3 months, 58 patients at 6 months, 47 patients at 12 months and for 35 patients at 24 months. The

reason data was not available for the remaining patients was that patients had either not reached the relevant time interval, were lost to follow-up (3 cases, 2 at 12 and 1 at 24 months) or had died (1 patient died between 3 months and 6 months follow-up).

Median age was 58 years (range 41–70 years). There were 38 male and 25 female patients. Twenty-two patients underwent bilateral LVRS, 8 by VATS and 14 by median sternotomy. 41 patients had unilateral VATS.

Postoperative change in pulmonary function

There was a significant postoperative improvement in FEV₁, TLC and RV lasting for at least 2 years post surgery (Table 1).

Postoperative change in health status

The best SF 36 scores were obtained 6 months after surgery (Fig. 1). At this time interval there was a statistically significant overall improvement in SF 36 scores in 7 out of the 8 health domains. The pain score at 6 months was still lower than the preoperative score.

As the influence of LVRS on each of the 8 domains of the SF 36 questionnaire is different we looked in each health domain how many patients improved their scores after surgery (responders (group R)) and how many showed no improvement or a worse score (non-responders (group NR)).

The relative distribution between the two groups varied according to health domain with the biggest group R in the domain of physical function (79% of patients with improved score) and the smallest group R in the pain domain (26% of patients with improved score) (Table 2). There was no difference between the R and NR groups as regard to age, gender, type of operation, preoperative weight or distribution of underweight patients.

Postoperative change in weight and body mass index

Preoperative weight was 63 (14) kg and BMI 22 (4) kg/m². Twelve patients were nutritional depleted (i.e. BMI less than 19 kg/m²). There was a postoperative increase in weight and BMI after LVRS, which was statistically significant from 6 month up to 24 months post surgery (Fig. 2).

There was no statistically significant correlation between the improvement in hyperinflation and the

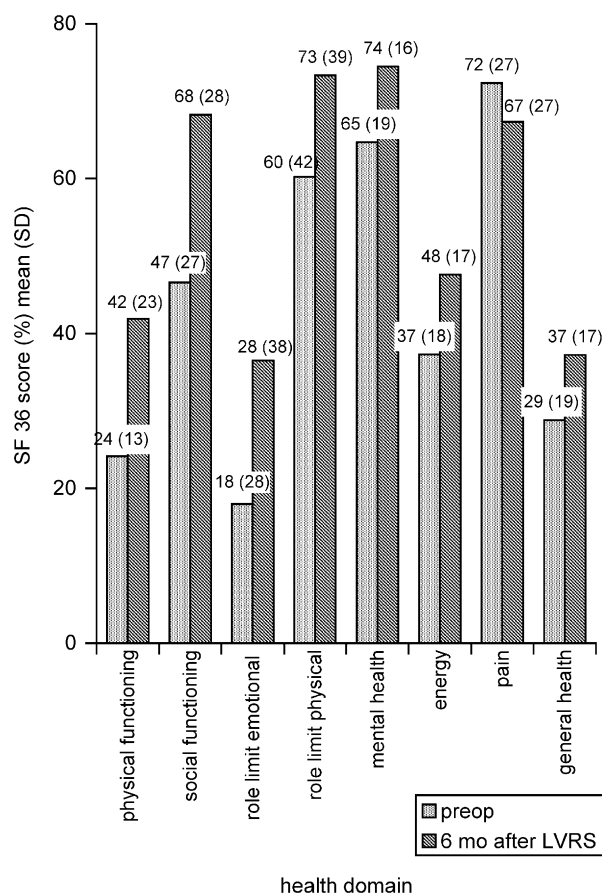


Figure 1 Health status assessed by SF 36 improves 6 months after LVRS in all domains except for pain (0% worse score, 100% best score).

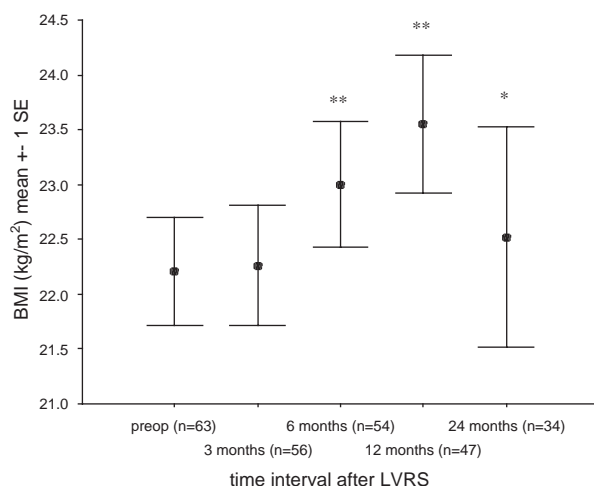
Table 1 Postoperative changes in pulmonary function.

Mean (SD)	Preop	3 months postop	6 months postop	12 months postop	24 months postop
No of patients	63	56	54	47	34
FEV ₁ (% pred)	28 (9)	35 (13)**	34 (14)**	35 (14)**	33 (13)
TLC (% pred)	146 (17)	127 (18)**	132 (17)**	133 (20)**	127 (15)**
RV (% pred)	267 (58)	208 (51)**	213 (55)**	220 (63)**	221 (56)**
DLCO (% pred)	45 (12)	45 (13)	47 (14)	45 (15)	47 (16)

** $P < 0.01$ paired t -test.

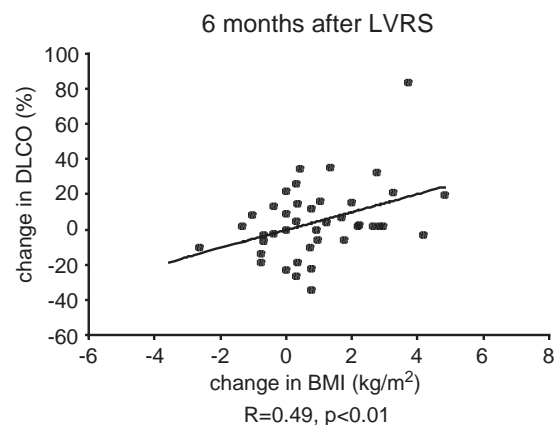
Table 2 Changes in BMI and their correlation with DLCO in group non-responders (NR) and responders (R).

Health domain		Ratio NR/R (%)	Change in BMI mean (SD) (kg/m ²)	Correlation with DLCO
Physical functioning	NR	21	0.3 (1.3)	$R = 0.34$
	R	79	0.6 (1.6)*	$R = 0.49^{**}$
Social functioning	NR	31	0.4 (1.1)	$R = 0.11$
	R	69	0.6 (1.6)*	$R = 0.49^*$
Role limit physical problems	NR	60	0.3 (1.5)	$R = 0.18$
	R	40	0.9 (1.4)*	$R = 0.62^{**}$
Role limit emot problems	NR	62	0.4 (1.3)	$R = 0.35$
	R	38	0.7 (1.7)	$R = 0.57^*$
Mental health	NR	33	0.3 (1.0)	$R = 0.03$
	R	67	0.7 (1.7)*	$R = 0.53^*$
Energy	NR	33	-0.2 (1.4)	$R = 0.15$
	R	67	0.9 (1.4)**	$R = 0.45^*$
Pain	NR	74	0.5 (1.6)*	$R = 0.49^{**}$
	R	26	0.5 (1.1)	$R = 0.15$
General health perception	NR	38	0.7 (1.3)*	$R = 0.29$
	R	62	0.4 (1.6)	$R = 0.55^{**}$

* $P < 0.05$.** $P < 0.01$.**Figure 2** Postoperative improvements in BMI after LVRS.* $P < 0.05$, ** $P < 0.01$ compared to preoperative values.

change in weight or BMI. However, we did find a significant correlation between the change in weight and BMI and change in DLCO at 6, 12 and 24 months (Fig. 3). There was a similar correlation with the changes in FEV₁ at 6, 12 and 24 months (Fig. 4). The best correlation was seen at 6 months.

Group R (Table 2): In six health domains, with the exceptions of the domains of pain and general

**Figure 3** Correlation between changes in BMI and changes in DLCO 6 months after LVRS.

health perception, group R showed significant increases in weight and BMI as well as DLCO. These changes in weight and BMI correlated with changes in DLCO. In these 6 domains the changes in FEV₁, TLC and RV were significant but there was no correlation between the changes in FEV₁ or hyperinflation and changes in BMI.

Group NR (Table 2): There was a significant improvement in weight and BMI in the pain and general health perception domain but not in the

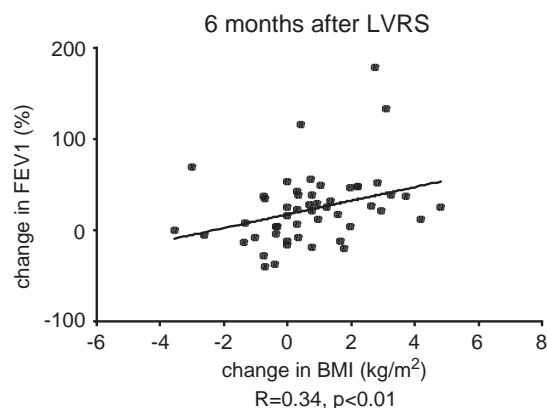


Figure 4 Correlation between changes in BMI and changes in FEV₁ 6 months after LVRS.

other domains. Although this group showed a significant reduction in TLC and RV, there was no significant improvement in DLCO. In four domains a significant improvement was found in FEV₁. There was no correlation between the changes in BMI and the changes in DLCO or changes in hyperinflation.

Discussion

LVRS significantly affects BMI, which correlates with changes in DLCO and may reflect changes in health status.

Patients with emphysema are frequently nutritionally depleted. However, less is known about the underlying mechanism. Nutritional depletion can result from an imbalance between energy intake and expenditure of energy and/or from an altered substrate metabolism.¹⁶

The improvements in nutritional status after LVRS may be due to increase in dietary intake. It may be that patients who feel less dyspnoeic after LVRS are more likely to eat more as eating causes less postprandial breathlessness.¹⁷ Improvement in health status may also result in patients to eat more. There may be a positive influence on diet intake from dieticians during patients' hospital stay. However, although Nezu did find an increase in dietary intake after LVRS, this did not correlate with the changes in weight.⁸ In addition, emphysema patients who underwent lung transplantation and who were nutritionally depleted preoperatively, also improved their nutritional status post surgery whilst maintaining their preoperative caloric intake.¹⁸

Another explanation of the observed improvement in weight is decreased resting energy expenditure. Takayama found reduced energy expenditure of the respiratory muscles, correlating

with the improvements in hyperinflation and small airway obstruction observed after LVRS.¹⁹ The increase in fat-free mass would also result in a more effective respiratory muscle function. Mineo did find a significant correlation between RV and the increase in weight after LVRS.⁹ However, Christensen also found no correlation between TLC or RV and the changes in weight.⁷ Baarends found that patients with COPD had an increased activity-related energy expenditure.²⁰ As patients gain fat-free mass after LVRS there may be a more efficient use of muscle mass resulting in decreased activity-related energy expenditure.

Loss of skeletal muscle mass has also been attributed to inflammatory mediators such as tumour necrosis factor α (TNF- α) and interleukins.²¹ In addition patients will develop an inflammatory response to their operation. Drugs as corticosteroids and smoking will modify this inflammatory response. The difference between the R and NR group may be related to a different inflammatory status. One study similarly showed that some underweight emphysematous patients did and some patients did not respond to nutritional therapy. This non-response was correlated with an elevated systemic inflammatory response.²²

Any explanation of the improved BMI after LVRS has to include the observed correlation with the changes in DLCO. Oxygen delivery may play a role in weight gain. Christensen's study looked into more detail in the possible mechanisms.⁷ The hypothesis that this was due to increased haemoglobin secondary to the improved nutritional status could not be confirmed as they observed a decrease rather than an increase in haemoglobin after LVRS. It was also suggested that DLCO improved due to opening of pulmonary vessels but there was no change in the postoperative KCO. The loss of fat-free mass in emphysematous patients has been linked to an altered protein metabolism. A consistent finding is the reduction in muscle glutamate, which has been associated with a reduction in diffusing capacity.²³

There is an influence of nutrition depletion on health status in patients with emphysema. Dyspnoea, reduced exercise capacity and reduced fat-free mass are thought to be related to health status.²⁴ Sahebajami found that underweight patients were more dyspnoeic than normal weight patients and that DLCO was a predictor of the dyspnoea intensity.³

The majority of our analysis is performed at 6 months post LVRS. The greatest improvement in health status (as measured with the SF 36 questionnaire) is at 6 months. After 6 months there is a steady decline in health status. This may represent

natural progression of the disease. The maximum increase in BMI occurs at 1 year, whilst pulmonary function starts declining after 3–6 months. The correlation between increase in BMI and DLCO might be greater if maximum BMI increase and maximum DLCO improvement were correlated even though they were measured at different time points.

We used the SF 36 questionnaire rather than a disease-specific instrument so that we could measure the impact of LVRS on the wider aspects of health status. Mahler's evaluation of the SF 36 in patients with COPD found it to be a valid instrument to measure health status in these patients, although as yet it is not known what change in score consists of a clinical significant change.²⁵

One problem in comparing studies on nutrition is that nutritional status is being defined in various different ways. We only used weight and BMI as parameter of nutrition. Although antropometric measurements and measurement of fat-free mass may be more accurate, weight and BMI is a more practical tool for assessing patients preoperatively and in out-patient clinics. In addition, it is BMI that has been linked to prognosis.⁴

Not only does nutritional depletion have an impact on the degree of dyspnoea and possibly health status, it is also a risk factor for post-operative complications after LVRS.^{26,27}

In this limited observational study we have found that successful LVRS is associated with improvement in nutritional status. Although we have not been able to explain the exact mechanism for this, it is reasonable to assume that performing LVRS has some positive benefit since simple nutritional supplementation is not associated with such improvement.

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